PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

To:
DR.BAKULESH MAFATLAL KHAMAR
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PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43*bis*.1)

Date of mailing *(day/month/year)*	05 JUN 2007
Applicant's or agent's file reference BMK-PCT-APRIL06	FOR FURTHER ACTION See paragraph 2 below

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/IB06/00978	21 April 2006 (21.04.2006)	25 April 2005 (25.04.2005)

International Patent Classification (IPC) or both national classification and IPC

IPC(8): C12N 1/20(2006.01)
USPC: 435/253.1

Applicant

DR. BAKULESH MAFATLAL KHAMAR

1. This opinion contains indications relating to the following items:

- ☒ Box No. I — Basis of the opinion
- ☐ Box No. II — Priority
- ☒ Box No. III — Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV — Lack of unity of invention
- ☒ Box No. V — Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI — Certain documents cited
- ☐ Box No. VII — Certain defects in the international application
- ☒ Box No. VIII — Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1*bis*(*b*) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

Name and mailing address of the ISA/ US	Date of completion of this opinion	Authorized officer
Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (571) 273-3201	02 May 2007 (02.05.2007)	Jeffrey Siew Telephone No. 571-272-0864

Form PCT/ISA/237 (cover sheet) (April 2005)

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International application No.
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Box No. I Basis of this opinion

1. With regard to the **language**, this opinion has been established on the basis of:

☒ the international application in the language in which it was filed

☐ a translation of the international application into _____, which is the language of a translation furnished for the purposes of international search (Rules 12.3(a) and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

☐ a sequence listing

☐ table(s) related to the sequence listing

b. format of material

☐ on paper

☐ in electronic form

c. time of filing/furnishing

☐ contained in the international application as filed.

☐ filed together with the international application in electronic form.

☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table(s) relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non-obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 4,10,12-21 and 26-28

because:

☐ the said international application, or the said claim Nos. _____ relate to the following subject matter which does not require an international search *(specify)*:

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. _____ are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. _____ are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☒ no international search report has been established for said claims Nos. 4,10,21-21 and 26-28 because they are improper multiple dependent claims and are not drafted in accordance with Rule 6.4(a).

☐ a meaningful opinion could not be formed without the sequence listing; the applicant did not, within the prescribed time limit:

- ☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Searching Authority in a form and manner acceptable to it.
- ☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b).

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-bis of the Administrative Instructions, and such tables were not available to the International Searching Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See Supplemental Box for further details.

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Box No. V Reasoned statement under Rule 43 *bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims NONE	YES
	Claims 1-3, 5-9, 11, 22-25, 29	NO
Inventive step (IS)	Claims NONE	YES
	Claims 1-3,5-9,11,22-25,29	NO
Industrial applicability (IA)	Claims 1-3,5-9,11,22-25,29	YES
	Claims NONE	NO

2. Citations and explanations:

Please See Continuation Sheet

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

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Box No. VIII Certain observations on the international application

The following observations on the clarity of the claims, description, and drawings or on the questions whether the claims are fully supported by the description, are made:

Claim 23 is objected to as lacking clarity under PCT Rule 66.2(a)(v) because of the claim is not fully supported by the description. The description does not disclose the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art because:

The claims are drawn to a composition comprising *Mycobacterium w* (*Mw*) and/or its constituent(s) as adjuvant and antigen(s) in a pharmaceutically acceptable carrier wherein said composition prevents diseases in a mammal by inducing or enhancing immunogenicity of antigen.

The nature of the invention is the use of an adjuvant and antigen composition to prevent disease by enhancing immunogenicity of said antigen. The claim is broad as the particular disease being prevented is not specified, thus prevention of all diseases of mammals by using said composition comprising *Mw* adjuvant and any antigen. Such diseases include those due to infections, genetic diseases, diseases due to cancer etc. The scope of all diseases of mammals is extremely broad.

The disclosure does not teach the prevention of any disease of mammals using the claimed composition. The disclosure teaches the adjuvant effect of *Mw* when co-administered in healthy individuals with known vaccines containing bacterial or viral antigens or cancer antigens (p. 15-17). The adjuvant effect allows for increased antibody titers in both humans and mice tested. However, there is no correlation of these results with the prevention of any disease. The art is silent as to the prevention of all diseases of mammals with any adjuvant containing composition. As to infectious diseases, adjuvants in general improve the efficacy of vaccines for prevention of certain infections (see Petrovsky) but not all infections. The efficacy of the instant composition for prevention of diseases due to genetic errors is however unpredictable, as the disclosure (and the art) lack a correlation between the administration of said composition (or adjuvants in general) and prevention of such diseases.

In view of the above, Applicant(s) have not disclosed the claimed invention in a manner sufficiently clear and complete for the claimed invention to be carried out by a person skilled in the art

Supplemental Box
In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 1-3, 5-9, 11, 22-25 and 29 lack novelty under PCT Article 33(2) as being anticipated by Modi et al, WO 03/075825 18 September 2003.

Modi et al teach a composition comprising *Mycobacterium w* (Mw) and antigens (*Mw* cell constituents) in a pharmaceutically acceptable carrier (p. 5-9 and p. 11 2nd to the last paragraph). The composition of Modi et al further contains other adjuvants (p. 19 claim 33) and said *Mw* is killed by heat radiation in the form of autoclaving (p.5, p. 17 claim 11). Modi teaches constituents/antigens of *Mw* are obtained by sonication, high pressure fractionator, osmotic pressure ingredient, by extraction with organic solvents or by enzymatic treatment e.g. lyticase or pronase (p.11). Since the composition of Modi et al and the instantly claimed composition are the same, the *Mw* in the composition of Modi et al will also act as an adjuvant and will elicit enhanced immune response to the *Mw* cell wall antigens and when administered to a mammal will induce or enhance immunogenicity thus leading to decreased morbidity and mortality.

Claims 1-3, 5-9, 11, 22-25 and 29 lack novelty under PCT Article 33(2) as being anticipated by Khamar et al. WO 03/049667 19 June 2003.

Khamar et al teach a composition comprising *Mycobacterium w* (*Mw*) and antigens (*Mw* cell constituents) in a pharmaceutically acceptable carrier (p. 7 see J). The composition of Khamar et al further contains other adjuvants (p. 15 claims 1 and 8) and said *Mw* is killed by heat radiation in the form of autoclaving (p.15 claim 3, p. 10). Khamar teaches constituents/antigens of *Mw* are obtained by sonication, high pressure fractionator, osmotic pressure ingredient, by extraction with organic solvents or by enzymatic treatment e.g. lyticase or pronase (p.10). Since the composition of Khamar et al and the instantly claimed composition are the same, the *Mw* in the composition of Khamar et al will also act as an adjuvant and will elicit enhanced immune response to the Mw cell wall antigens and when administered to a mammal will induce or enhance immunogenicity thus leading to decreased morbidity and mortality.

Claims 1-3, 5-9, 11, 22, 24, 25 and 29 lack an inventive step under PCT Article 33(3) as being obvious over Modi et al, WO 03/075825 18 September 2003 in view of Petrovsky et al. Immunology and Cell Biology, 2004, 82:488-496.

Modi et al teach a composition comprising *Mycobacterium w* (*Mw*) and antigens (*Mw* cell constituents) in a pharmaceutically acceptable carrier (p. 5-9 and p. 11 2nd to the last paragraph). The composition of Modi et al further contains other adjuvants (p. 19 claim 33) and said *Mw* is killed by heat radiation in the form of autoclaving (p.5, p. 17 claim 11). Modi teaches constituents/antigens of *Mw* are obtained by sonication, high pressure fractionator, osmotic pressure ingredient, by extraction with organic solvents or by enzymatic

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Modi et al does not teach a composition comprising constituents of *Mw* as adjuvant and non- Mycobacterial antigens.

Petrovsky et al teach that adjuvants are compounds that enhance the specific immune response against co-inoculated antigens (see under adjuvant origins and adjuvant roles p. 488). Petrovsky teach that constituents of *Mycobacterium* spp e.g. MDP as adjuvant (p. 490 under bacteria derived antigens).

It would have been obvious to one of skill in the art at the time of the invention to include in the composition of Modi et al comprising constituents of Mw as adjuvant, non-Mycobacterial antigens as taught by Petrovsky et al. The motivation to do so is provided by Petrovsky et al who teaches that constituents of *Mycobacterium* spp act as adjuvant and that adjuvant enhance the specific immune response against co-inoculated antigens.

Claims 1-3, 5-9, 11, 22, 24,25 and 29 lack an inventive step under PCT Article 33(3) as being obvious over by Khamar et al. WO 03/049667 19 June 2003 in view of Petrovsky et al. Immunology and Cell Biology, 2004, 82:488-496.

Khamar et al teach a composition comprising *Mycobacterium w* (*Mw*) and antigens (*Mw* cell constituents) in a pharmaceutically acceptable carrier (p. 7 see J). The composition of Khamar et al further contains other adjuvants (p. 15 claims 1 and 8) and said Mw is killed by heat radiation in the form of autoclaving (p.15 claim 3, p. 10). Khamar teaches constituents/antigens of *Mw* are obtained by sonication, high pressure fractionator, osmotic pressure ingredient, by extraction with organic solvents or by enzymatic treatment e.g. lyticase or pronase (p.10). Since the composition of Khamar et al and the instantly claimed composition are the same, the *Mw* in the composition of Khamar et al will also act as an adjuvant and will elicit enhanced immune response to the *Mw* cell wall antigens and when administered to a mammal will induce or enhance immunogenicity thus leading to decreased morbidity and mortality.

Khamar et al does not teach a composition comprising constituents of *Mw* as adjuvant and non- Mycobacterial antigens.

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It would have been obvious to one of skill in the art at the time of the invention to include in the composition of Khamar et al comprising constituents of *Mw* as adjuvant, non-Mycobacterial antigens as taught by Petrovsky et al. The motivation to do so is provided by Petrovsky et al who teaches that constituents of *Mycobacterium* spp act as adjuvant and that adjuvant enhance the specific immune response against co-inoculated antigens.

Claims 1-3, 5-9, 11, 22-25 and 29 have industrial applicability as defined by PCT Article 33(4) as the invention encompassed by the claims can be used in industry.